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Figure 1

Pfu	10	20	30	40	50	60
DeepVent	MILDVDYITEEDGKPIIRL	EKKENGKFKI	EHDRTRFRPYIYALL	RDDSK	IEVVKKITG	ERHGG
Hybrid_design	MILDADYITEEDGKPIIRI	EKKENGGEFKVEY	DRNFRPYIYALLKDDSQ	IDEVVRKITA	ERHGG	
	MILDXDYITEEXGKPIIRX	EKKENGXFKXEX	DRXFRPYIYALLXDDSX	IXEVVKKITX	ERHGG	

Pfu	70	80	90	100	110	120
DeepVent	KIVRIIVDVVEKVEKVKFLGKPI	TVWKL	YLEHPPQDVPT	IRDKIREHSAVI	DIFFEYDIPFAKRY	
Hybrid_design	KIVRIIDAEKVRKVKFLGRPI	EVWRLYFFEHPPQDVPA	IRDKIREHSAVI	DIFFEYDIPFAKRY		
	KIVRIIXDXEKVXKVKFLGXPI	XVWXL	YXEHPPQDVPPX	IRXKXREHSAVX	DIFFEYDIPFAKRY	

Pfu	130	140	150	160	170	180
DeepVent	LIDKGLIPMEGEGEELKILAF	DIETLYHEGEEFFGKGP	IMISYADENEAKVITWK	NI	IDL	PPY
Hybrid_design	LIDKGLIPMEGDEELKLLAF	DIETLYHEGEEFFAKGP	IMISYADENEAKVITWK	KI	IDL	PPY
	LIDKGLIPMEGXEEELKXLA	FDIETLYHEGEEFFXKGP	IMISYADENEAKVITWK	XI	IDL	PPY

Pfu	190	200	210	220	230	240
DeepVent	VEVVSSEMEREMIKRFLRI	IREKDDPDII	IVTYNGDSFDFPYLLAKRAE	KLGIKL	TI	GRDGSSEPK
Hybrid_design	VEVVSSEMEREMIKRFLKVI	IREKDDPDVII	TYNGDSFDFPYLVKRAE	KLGIKL	PL	GRDGSSEPK
	VEVVSSEMEREMIKRFLXXI	IREKDDPDXXI	TYNGDSFDFPYLVKRAE	KLGIKL	XX	GRDGSSEPK

Pfu	250	260	270	280	290	300
DeepVent	MQRIGDMTAVEVKGRIFHFDLYHVI	RTINLPTTYTLEAVYEA	IFGKPK	KEVYA	DEIA	KAW
Hybrid_design	MQRIGDMTAVEIKGRIFHFDLYHVI	RTINLPTTYTLEAVYEA	IFGKPK	KEVYA	HEIA	EAW
	MQRIGDMTAVEKGRIFHFDLYHVI	RTINLPTTYTLEAVYEA	IFGKPK	KEVYA	XX	EAW

Pfu	310	320	330	340	350	360
DeepVent	SGENLERVAKYSMEDAKA	ATYELGKEFFL	PMEIQLSRLV	GQPLWDV	SRSSTGNL	VWFWFLLRK
Hybrid_design	TGKGLERVAKYSMEDAKV	TYELGREFFL	PMEAQLSRLV	GQPLWDV	SRSSTGNL	VWFWFLLRK
	XGXLERVAKYSMEDAKX	TYELGXEFFL	PMEXQLSRLV	GQPLWDV	SRSSTGNL	VWFWFLLRK

Pfu	370	380	390	400	410	420
DeepVent	AYERNELVAPNKPSPSE	EYQRRRLRESY	TGGFFVKEPEKGLWE	NI	YLD	DFRSLYPSIITHNV
Hybrid_design	AYERNELVAPNKPSPSE	EYQRRRLRESY	TGGFFVKEPEKGLWE	NI	YLD	DFRSLYPSIITHNV
	AYERNELVAPNKPSPSE	EYQRRRLRESY	TGGFFVKEPEKGLWE	NI	YLD	DFRSLYPSIITHNV

Pfu	430	440	450	460	470	480
DeepVent	PDTLNLLEGCKNYDIA	PPQVGHKFCCKD	IPGFFIP	PSLL	GHLL	IEEROKIKITKMKETQDP
Hybrid_design	PDTLNLLEGCKREYDVA	PEVGHKFCCKD	PPGFFIP	PSLL	KRLLD	ERQEIKRKMKASKDP
	PDTLNLLEGCKXNYDXA	PPXVGHKFCCKD	XXPGFFIP	PSLL	XXLL	XXKMKXXXXDP

Figure 1 (cont'd)

Hybrid_design

DYRQK	L	L	A	N	S	F	Y	G	Y	G	Y	A	K	A	R	W	Y	C	K	E	C	A	E	S	V	T	A	W	G	R	K	Y	I	E	L	V	W	K	E	L	E	E	K	F	F	K	V	L	Y	I		
DYRQR	A	I	K	I	L	A	N	S	Y	Y	G	Y	A	K	A	R	W	Y	C	K	E	C	A	E	S	V	T	A	W	G	R	E	Y	I	E	F	V	R	K	E	L	E	E	K	F	F	K	V	L	Y	I	
DYRQX	A	I	K	X	L	A	N	S	X	Y	G	Y	A	K	A	R	W	Y	C	K	E	C	A	E	S	V	T	A	W	G	R	X	Y	I	E	X	V	I	X	K	E	L	E	E	K	F	F	K	V	L	Y	I

Pfu
 DeepVent
 Hybrid_design

D	T	D	G	L	Y	A	T	I	P	G	G	S	E	E	I	K	K	K	A	L	E	F	V	K	Y	I	N	S	K	L	P	G	L	L	E	L	E	E	Y	E	G	F	F	Y	K	R	G	F	F	V	T	K	K	R	Y	A	V	I	D	E	
D	T	D	G	L	Y	A	T	I	P	G	A	K	P	E	E	I	K	K	K	A	L	E	F	V	D	Y	I	N	A	K	L	P	G	L	L	E	L	E	E	Y	E	G	F	F	Y	V	R	G	F	F	V	T	K	K	K	Y	A	L	I	D	E
D	T	D	G	L	Y	A	T	I	P	G	X	X	X	E	E	I	K	K	K	A	L	E	F	V	K	Y	I	N	X	K	L	P	G	L	L	E	L	E	E	Y	E	G	F	F	Y	X	R	G	F	F	V	T	K	K	X	Y	A	X	I	D	E

[illegible]

pfu
 DeepVent
 Hybrid_design

L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	K	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E					
L	V	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	R	L	A	A	R	L	A	A	R	G	V	K	V	R	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	K	R	A	I	L	A	E	E	
L	X	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	X	L	A	A	X	X	L	A	A	X	G	V	K	X	X	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	X	R	A	I	L	A	E	E

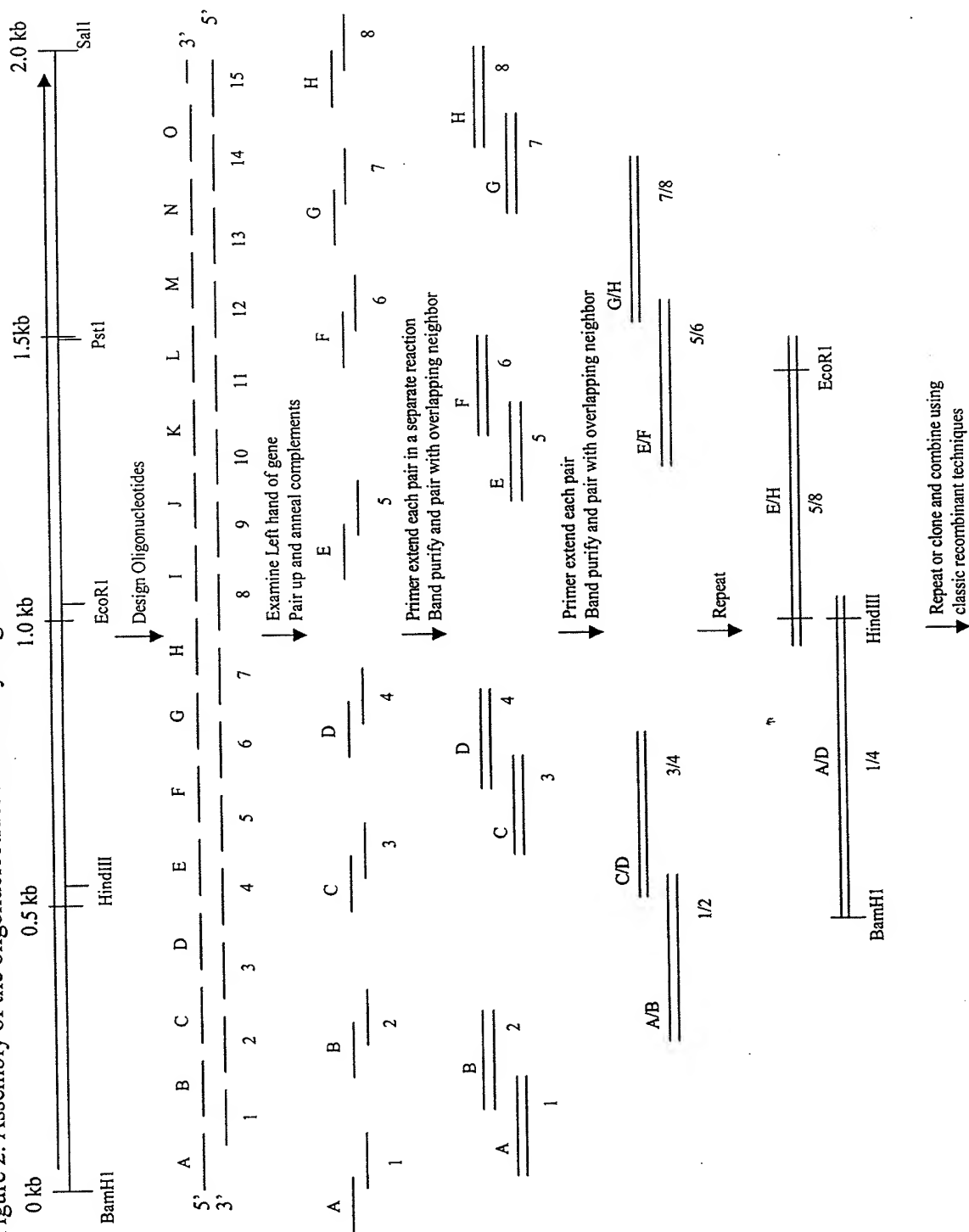
Pfu
 DeepVent
 Hybrid_design

YD	PK	KHKYD	AEY	IEN	QVL	PA	VL	R	I	E	G	F	G	Y	R	K	E	D	L	R	Y	Q	K	T	R	Q	V	G	L	T	S	W	L	N	I	K	K	S					
FD	LR	KHKYD	AEY	IEN	QVL	PA	VL	R	I	E	A	F	G	Y	R	K	E	D	L	R	W	Q	K	T	K	Q	T	G	L	T	A	W	L	N	I	K	K						
XD	XX	KHKYD	AEY	IEN	QVL	PA	VL	R	I	E	X	F	G	Y	R	K	E	D	L	R	X	Q	K	T	X	Q	X	G	L	T	X	W	L	N	I	K	K	S	G	T	H	N	C

Pfu
DeepVent
Hybrid_design

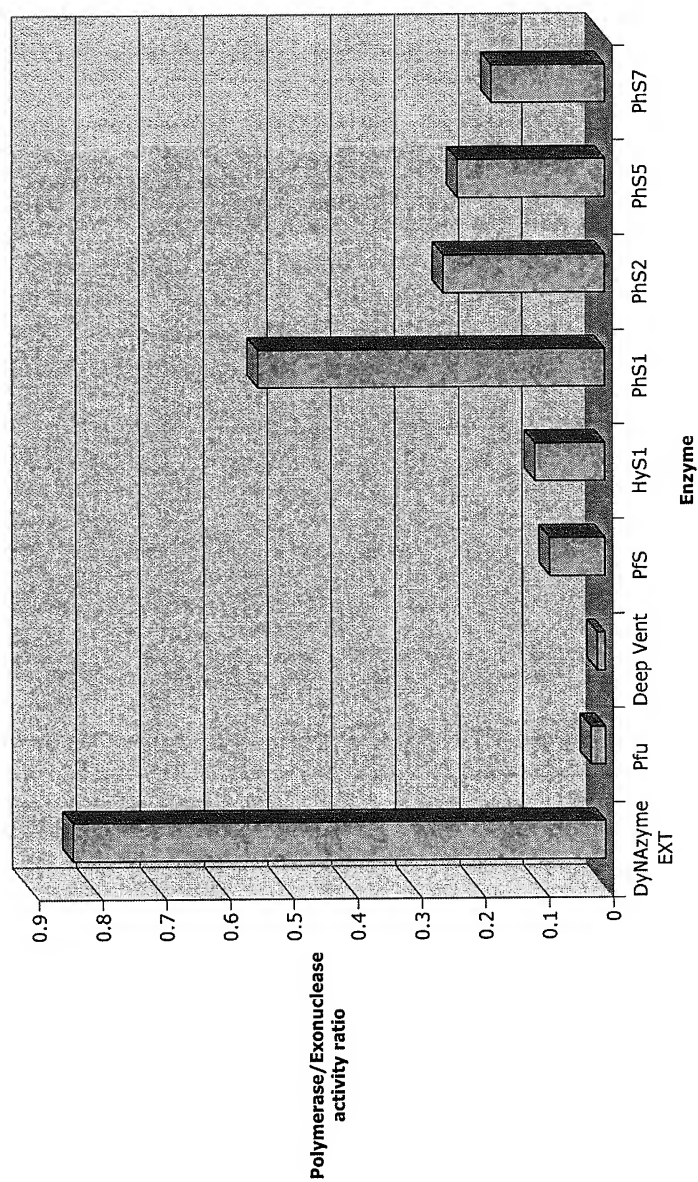
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Figure 2. Assembly of the oligonucleotides into library fragments.



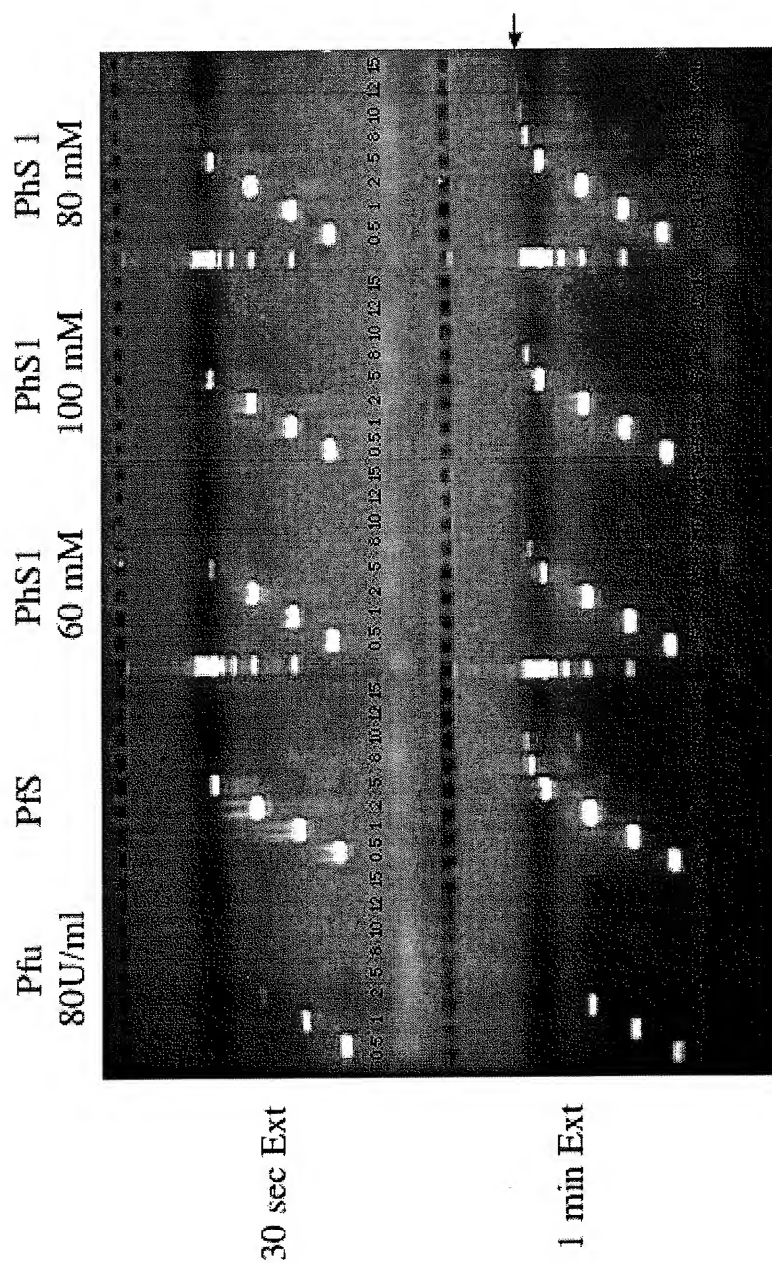
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Figure 3. A comparison of the polymerase to 3' to 5' exonuclease activity



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FIGURE 4



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Figure 5

Pfu	10	20	30	40	50	60
DeepVent	MIL	DDV	DDY	ITE	EEG	KPP
Hybrid_design	MIL	DDV	DDY	ITE	EEG	KPP
HyS1	MIL	DDV	DDY	ITE	EEG	KPP
Hyb2	MIL	DDV	DDY	ITE	EEG	KPP
Hyb3	MIL	DDV	DDY	ITE	EEG	KPP
HyS4	MIL	DDV	DDY	ITE	EEG	KPP
PhS1	MIL	DDV	DDY	ITE	EEG	KPP
PhS2	MIL	DDV	DDY	ITE	EEG	KPP
PhS3	MIL	DDV	DDY	ITE	EEG	KPP
PhS4	MIL	DDV	DDY	ITE	EEG	KPP
PhS5	MIL	DDV	DDY	ITE	EEG	KPP
PhS6	MIL	DDV	DDY	ITE	EEG	KPP
PhS7	MIL	DDV	DDY	ITE	EEG	KPP

Pfu	70	80	90	100	110	120
DeepVent	KIV	RIV	DDV	DDY	ITE	EEG
Hybrid_design	KIV	RIV	DDV	DDY	ITE	EEG
HyS1	KIV	RIV	DDV	DDY	ITE	EEG
Hyb2	KIV	RIV	DDV	DDY	ITE	EEG
Hyb3	KIV	RIV	DDV	DDY	ITE	EEG
HyS4	KIV	RIV	DDV	DDY	ITE	EEG
PhS1	KIV	RIV	DDV	DDY	ITE	EEG
PhS2	KIV	RIV	DDV	DDY	ITE	EEG
PhS3	KIV	RIV	DDV	DDY	ITE	EEG
PhS4	KIV	RIV	DDV	DDY	ITE	EEG
PhS5	KIV	RIV	DDV	DDY	ITE	EEG
PhS6	KIV	RIV	DDV	DDY	ITE	EEG
PhS7	KIV	RIV	DDV	DDY	ITE	EEG

Pfu
DeepVent
Hybrid_design
HyS1
Hyb2
Hyb3
HyS4
PhS1
PhS2
PhS3
PhS4
PhS5
PhS6
PhS7

Pfu
DeepVent
Hybrid_design
HyS1
Hyb2
Hyb3
HyS4
PhS1
PhS2
PhS3
PhS4
PhS5
PhS6
PhS7

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Figure 5 (cont'd)

Pfu	250	260	270	280	290	300
DeepVent	IGDMT	AVEV	KGR	IHF	DL	YHVI
Hybrid_design	IGDMT	AVEV	KGR	IHF	DL	YHVI
HyS1	IGDMT	AVEV	KGR	IHF	DL	YHVI
Hyb2	IGDMT	AVEV	KGR	IHF	DL	YHVI
Hyb3	IGDMT	AVEV	KGR	IHF	DL	YHVI
HyS4	IGDMT	AVEV	KGR	IHF	DL	YHVI
PhS1	IGDMT	AVEV	KGR	IHF	DL	YHVI
PhS2	IGDMT	AVEV	KGR	IHF	DL	YHVI
PhS3	IGDMT	AVEV	KGR	IHF	DL	YHVI
PhS4	IGDMT	AVEV	KGR	IHF	DL	YHVI
PhS5	IGDMT	AVEV	KGR	IHF	DL	YHVI
PhS6	IGDMT	AVEV	KGR	IHF	DL	YHVI
PhS7	IGDMT	AVEV	KGR	IHF	DL	YHVI

Pfu	310	320	330	340	350	360
DeepVent	LER	VAKY	SME	DAK	AT	YEL
Hybrid_design	LER	VAKY	SME	DAK	AT	YEL
HyS1	LER	VAKY	SME	DAK	AT	YEL
Hyb2	LER	VAKY	SME	DAK	AT	YEL
Hyb3	LER	VAKY	SME	DAK	AT	YEL
HyS4	LER	VAKY	SME	DAK	AT	YEL
PhS1	LER	VAKY	SME	DAK	AT	YEL
PhS2	LER	VAKY	SME	DAK	AT	YEL
PhS3	LER	VAKY	SME	DAK	AT	YEL
PhS4	LER	VAKY	SME	DAK	AT	YEL
PhS5	LER	VAKY	SME	DAK	AT	YEL
PhS6	LER	VAKY	SME	DAK	AT	YEL
PhS7	LER	VAKY	SME	DAK	AT	YEL

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Figure 5 (cont'd)

Pfu	370	AYERNEL	EVAPNKKPS	EE	EYER	QRRRL	RRRLRES	YTG	GGFF	VKEPE	KGLWEN	IVYLD	DFRSL	YPPS	II	ITHNVS	420
DeepVent		AYERNEL	LAPNKKPD	EX	EYER	RRRL	RRRLRES	YAG	GGFF	VKEPE	KGLWE	GLVSL	DFRSL	YPPS	II	ITHNVS	
Hybrid_design		AYERNEL	EXAPNKKPD	EX	EYER	RRRL	RRRLRES	YX	GGFF	VKEPE	KGLWE	XXVXL	DFRSL	YPPS	II	ITHNVS	
HyS1		AYERNEL	EVAPNKKPY	ER	EYER	RRRL	RRRLRES	YTG	GGFF	VKEPE	KGLWE	SLVSL	DFRSL	YPPS	II	ITHNVS	
Hyb2		AYERNEL	EVAPNKKPA	EQ	EYER	RRRL	RRRLRES	YTG	GGFF	VKEPE	KGLWE	DLVSL	DFRSL	YPPS	II	ITHNVS	
Hyb3		AYERNEL	EVAPNKKPA	EQ	EYER	RRRL	RRRLRES	YTG	GGFF	VKEPE	KGLWE	DLVSL	DFRSL	YPPS	II	ITHNVS	
HyS4		AYERNEL	EVAPNKKPA	EQ	EYER	RRRL	RRRLRES	YTG	GGFF	VKEPE	KGLWE	DLVSL	DFRSL	YPPS	II	ITHNVS	
PhS1		AYERNEL	EVAPNKKPD	ER	EYER	RRRL	RRRLRES	YAG	GGFF	VKEPE	KGLWE	IVYLD	DFRSL	YPPS	II	ITHNVS	
PhS2		AYERNEL	EVAPNKKPS	ER	EYER	RRRL	RRRLRES	YTG	GGFF	VKEPE	KGLWE	IVYLD	DFRSL	YPPS	II	ITHNVS	
PhS3		AYERNEL	EVAPNKKP	SE	EYER	RRRL	RRRLRES	YAG	GGFF	VKEPE	KGLWE	IVYLD	DFRSL	YPPS	II	ITHNVS	
PhS4		AYERNEL	EVAPNKKPD	DE	EYER	RRRL	RRRLRES	YTG	GGFF	VKEPE	KGLWE	IVYLD	DFRSL	YPPS	II	ITHNVS	
PhS5		AYERNEL	EVAPNKKPD	DE	EYER	RRRL	RRRLRES	YTG	GGFF	VKEPE	KGLWE	IVYLD	DFRSL	YPPS	II	ITHNVS	
PhS6		AYERNEL	EVAPNKKPD	DE	EYER	RRRL	RRRLRES	YTG	GGFF	VKEPE	KGLWE	IVYLD	DFRSL	YPPS	II	ITHNVS	
PhS7		AYERNEL	EVAPNKKPD	DE	EYER	RRRL	RRRLRES	YTG	GGFF	VKEPE	KGLWE	IVYLD	DFRSL	YPPS	II	ITHNVS	

Pfu	430	PDTLN	LEGGCK	NYDIA	PIQ	VGHK	FKCKD	IP	GGFF	IPSL	LGLLE	ERQK	IKT	KMKE	Q	PIEK	MLL	480
DeepVent		PDTLN	REGGCK	REYDV	AP	EVGHK	FKCKD	PP	GGFF	IPSL	LGLLE	ERQK	IKR	KMKE	AS	DDPIEK	MLL	
Hybrid_design		PDTLN	REGGCK	XXYDV	AP	EVGHK	FKCKD	XX	PPGGFF	IPSL	LGLLE	ERQK	IKX	KMKE	XX	DDPIEK	MLL	
HyS1		PDTLN	REGGCK	DDYDI	AP	EVGHK	FKCKD	DF	LGFF	IPSL	LGLLE	ERQK	IKT	KMKE	ET	XXDDPIEK	MLL	
Hyb2		PDTLN	REGGCK	DDYDI	AP	EVGHK	FKCKD	DF	LGFF	IPSL	LGLLE	ERQK	IKT	KMKE	ET	XXDDPIEK	MLL	
Hyb3		PDTLN	REGGCK	DDYDI	AP	EVGHK	FKCKD	DF	LGFF	IPSL	LGLLE	ERQK	IKT	KMKE	ET	XXDDPIEK	MLL	
HyS4		PDTLN	REGGCK	DDYDI	AP	EVGHK	FKCKD	DF	LGFF	IPSL	LGLLE	ERQK	IKT	KMKE	ET	XXDDPIEK	MLL	
PhS1		PDTLN	REGGCK	DDYDV	AP	EVGHK	FKCKD	DF	LGFF	IPSL	LGLLE	ERQK	IKT	KMKE	AS	DDPIEK	MLL	
PhS2		PDTLN	LEGGCK	REYDV	AP	EVGHK	FKCKD	IT	PPGGFF	IPSL	LGLLE	ERQK	IKR	KMKE	AS	DDPIEK	MLL	
PhS3		PDTLN	REGGCK	REYDV	AP	EVGHK	FKCKD	IT	PPGGFF	IPSL	LGLLE	ERQK	IKR	KMKE	AS	DDPIEK	MLL	
PhS4		PDTLN	REGGCK	REYDV	AP	EVGHK	FKCKD	FF	PPGGFF	IPSL	LGLLE	ERQK	IKR	KMKE	AS	DDPIEK	MLL	
PhS5		PDTLN	REGGCK	REYDV	AP	EVGHK	FKCKD	FF	PPGGFF	IPSL	LGLLE	ERQK	IKR	KMKE	AS	DDPIEK	MLL	
PhS6		PDTLN	REGGCK	REYDV	AP	EVGHK	FKCKD	FF	PPGGFF	IPSL	LGLLE	ERQK	IKR	KMKE	AS	DDPIEK	MLL	
PhS7		PDTLN	REGGCK	REYDV	AP	EVGHK	FKCKD	FF	PPGGFF	IPSL	LGLLE	ERQK	IKT	KMKE	AT	KKDDPIEK	MLL	

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Figure 5 (cont'd)

Pfu	490	DYRQKAIKLLANSFYGYGYAKARWYCKECAESVTAWGRKYLELVWKELEEEKFPGFKVLYI	500	510	520	530	540
DeepVent		RRAIKLLANSFYGYGYAKARWYCKECAESVTAWGRKYLELVWKELEEEKFPGFKVLYI					
Hybrid_design		RAIKLLANSFYGYGYAKARWYCKECAESVTAWGRKYLELVWKELEEEKFPGFKVLYI					
HyS1		DYRQKAIKLLANSFYGYGYAKARWYCKECAESVTAWGRKYLELVWKELEEEKFPGFKVLYI					
Hyb2		DYRQKAIKLLANSFYGYGYAKARWYCKECAESVTAWGRKYLELVWKELEEEKFPGFKVLYI					
Hyb3		DYRQKAIKLLANSFYGYGYAKARWYCKECAESVTAWGRKYLELVWKELEEEKFPGFKVLYI					
HyS4		DYRQKAIKLLANSFYGYGYAKARWYCKECAESVTAWGRKYLELVWKELEEEKFPGFKVLYI					
PhS1		DYRQKAIKLLANSFYGYGYAKARWYCKECAESVTAWGRKYLELVWKELEEEKFPGFKVLYI					
PhS2		DYRQKAIKLLANSFYGYGYAKARWYCKECAESVTAWGRKYLELVWKELEEEKFPGFKVLYI					
PhS3		DYRQRAIKLLANSFYGYGYAKARWYCKECAESVTAWGRKYLELVWKELEEEKFPGFKVLYI					
PhS4		DYRQRAIKLLANSFYGYGYAKARWYCKECAESVTAWGRKYLELVWKELEEEKFPGFKVLYI					
PhS5		DYRQRAIKLLANSFYGYGYAKARWYCKECAESVTAWGRKYLELVWKELEEEKFPGFKVLYI					
PhS6		DYRQRAIKLLANSFYGYGYAKARWYCKECAESVTAWGRKYLELVWKELEEEKFPGFKVLYI					
PhS7		DYRQRAIKLLANSFYGYGYAKARWYCKECAESVTAWGRKYLELVWKELEEEKFPGFKVLYI					
Pfu	550	DTDGLYATIPGGESIEIKKKALEFFVKYINAKLPGLLELEVEYEGFYKRGFFVTKKRYAVIDE	560	570	580	590	600
DeepVent		DTDGLYATIPGGKPEIEIKKKALEFFVKYINAKLPGLLELEVEYEGFYKRGFFVTKKRYAVIDE					
Hybrid_design		DTDGLYATIPGGKPEIEIKKKALEFFVKYINAKLPGLLELEVEYEGFYKRGFFVTKKRYAVIDE					
HyS1		DTDGLYATIPGGKPEIEIKKKALEFFVKYINAKLPGLLELEVEYEGFYKRGFFVTKKRYAVIDE					
Hyb2		DTDGLYATIPGGKPEIEIKKKALEFFVKYINAKLPGLLELEVEYEGFYKRGFFVTKKRYAVIDE					
Hyb3		DTDGLYATIPGGKPEIEIKKKALEFFVKYINAKLPGLLELEVEYEGFYKRGFFVTKKRYAVIDE					
HyS4		DTDGLYATIPGGKPEIEIKKKALEFFVKYINAKLPGLLELEVEYEGFYKRGFFVTKKRYAVIDE					
PhS1		DTDGLYATIPGGKPEIEIKKKALEFFVKYINAKLPGLLELEVEYEGFYKRGFFVTKKRYAVIDE					
PhS2		DTDGLYATIPGGKPEIEIKKKALEFFVKYINAKLPGLLELEVEYEGFYKRGFFVTKKRYAVIDE					
PhS3		DTDGLYATIPGGKPEIEIKKKALEFFVKYINAKLPGLLELEVEYEGFYKRGFFVTKKRYAVIDE					
PhS4		DTDGLYATIPGGKPEIEIKKKALEFFVKYINAKLPGLLELEVEYEGFYKRGFFVTKKRYAVIDE					
PhS5		DTDGLYATIPGGKPEIEIKKKALEFFVKYINAKLPGLLELEVEYEGFYKRGFFVTKKRYAVIDE					
PhS6		DTDGLYATIPGGKPEIEIKKKALEFFVKYINAKLPGLLELEVEYEGFYKRGFFVTKKRYAVIDE					
PhS7		DTDGLYATIPGGKPEIEIKKKALEFFVKYINAKLPGLLELEVEYEGFYKRGFFVTKKRYAVIDE					

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Figure 5 (cont'd)

Pfu	610	EGK	VI	TR	GLE	E	IV	RR	DW	SE	E	I	A	K	E	T	Q	A	R	V	L	E	I	L	K	H	G	N	V	E	E	A	V	R	I	V	K	E	V	I	Q	K	L	A	N	Y	E	I	P	P	E	K	620	
DeepVent		EGK	I	TR	GLE	E	IV	RR	DW	SE	E	I	A	K	E	T	Q	A	R	V	L	E	I	L	K	H	G	N	V	E	E	A	V	R	I	V	K	E	V	I	Q	K	L	S	K	Y	E	I	P	P	E	K	630	
Hybrid_design		EGK	X	I	TR	GLE	E	IV	RR	DW	SE	E	I	A	K	E	T	Q	A	R	V	L	E	X	I	L	K	H	G	N	V	E	E	A	V	X	I	V	K	E	V	I	Q	K	L	X	Y	E	I	P	P	E	K	640
HyS1		EGK	I	TR	GLE	E	IV	RR	DW	SE	E	I	A	K	E	T	Q	A	R	V	L	E	I	L	K	H	G	N	V	E	E	A	V	K	I	V	K	E	I	I	E	K	L	A	K	Y	E	I	P	P	E	K	650	
Hyb2		EGK	I	TR	GLE	E	IV	RR	DW	SE	E	I	A	K	E	T	Q	A	R	V	L	E	I	L	K	H	G	N	V	E	E	A	V	K	I	V	K	E	I	I	E	K	L	A	K	Y	E	I	P	P	E	K	660	
Hyb3		EGK	I	TR	GLE	E	IV	RR	DW	SE	E	I	A	K	E	T	Q	A	R	V	L	E	I	L	K	H	G	N	V	E	E	A	V	K	I	V	K	E	I	I	E	K	L	A	K	Y	E	I	P	P	E	K	670	
Hyb4		EGK	I	TR	GLE	E	IV	RR	DW	SE	E	I	A	K	E	T	Q	A	R	V	L	E	I	L	K	H	G	N	V	E	E	A	V	K	I	V	K	E	I	I	E	K	L	A	K	Y	E	I	P	P	E	K	680	
HyS4		EGK	I	TR	GLE	E	IV	RR	DW	SE	E	I	A	K	E	T	Q	A	R	V	L	E	I	L	K	H	G	N	V	E	E	A	V	K	I	V	K	E	I	I	E	K	L	A	K	Y	E	I	P	P	E	K	690	
PhS1		EGK	I	TR	GLE	E	IV	RR	DW	SE	E	I	A	K	E	T	Q	A	R	V	L	E	I	L	K	H	G	N	V	E	E	A	V	R	I	V	K	E	V	T	Q	K	L	S	K	Y	E	I	P	P	E	K	700	
PhS2		EGK	I	TR	GLE	E	IV	RR	DW	SE	E	I	A	K	E	T	Q	A	R	V	L	E	I	L	K	H	G	N	V	E	E	A	V	R	I	V	K	E	V	T	Q	K	L	A	K	Y	E	I	P	P	E	K	710	
PhS3		EGK	I	TR	GLE	E	IV	RR	DW	SE	E	I	A	K	E	T	Q	A	R	V	L	E	I	L	K	H	G	N	V	E	E	A	V	R	I	V	K	E	V	T	Q	K	L	S	N	Y	E	I	P	P	E	K	720	
PhS4		EGK	I	TR	GLE	E	IV	RR	DW	SE	E	I	A	K	E	T	Q	A	R	V	L	E	I	L	K	H	G	N	V	E	E	A	V	K	I	V	K	E	V	T	Q	K	L	A	K	Y	E	I	P	P	E	K	730	
PhS5		EGK	I	TR	GLE	E	IV	RR	DW	SE	E	I	A	K	E	T	Q	A	R	V	L	E	I	L	K	H	G	N	V	E	E	A	V	K	I	V	K	E	V	T	Q	K	L	A	K	Y	E	I	P	P	E	K	740	
PhS6		EGK	I	TR	GLE	E	IV	RR	DW	SE	E	I	A	K	E	T	Q	A	R	V	L	E	I	L	K	H	G	N	V	E	E	A	V	K	I	V	K	E	V	T	Q	K	L	A	K	Y	E	I	P	P	E	K	750	
PhS7		EGK	I	TR	GLE	E	IV	RR	DW	SE	E	I	A	K	E	T	Q	A	R	V	L	E	I	L	K	H	G	N	V	E	E	A	V	K	I	V	K	E	V	T	Q	K	L	A	K	Y	E	I	P	P	E	K	760	

pfu	670	L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	K	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	680	
DeepVent		L	V	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	R	L	A	A	R	G	V	K	V	R	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	K	R	A	I	L	A	E	E	690
Hybrid_design		L	X	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	X	L	A	A	X	G	V	K	X	X	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	X	R	A	I	L	A	E	E	700	
HyS1		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	K	R	A	I	L	A	E	E	710	
Hyb2		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	720	
Hyb3		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	730	
HyS4		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	K	R	A	I	L	A	E	E	740	
PhS1		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	750	
PhS2		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	760	
PhS3		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	R	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	770	
PhS4		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	V	R	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	780	
PhS5		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	V	R	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	790	
PhS6		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	V	R	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	800	
PhS7		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	V	R	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	810	

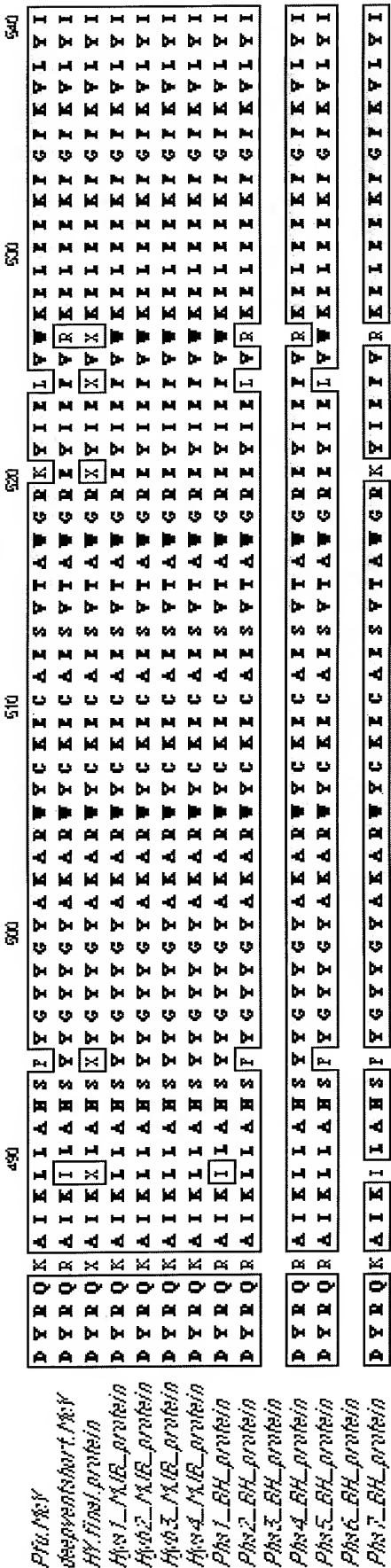
Figure 5 (cont'd)

	730	740	750	760	770	780
pfu	YD	PKKHKKYDAEYYIENQVLP	AVLRILE	GF	GYR	KEDLR
DeepVent	FD	LKKHKKYDAEYYIENQVLP	AVLRILE	AF	GYR	KEDLR
Hybrid_design	FD	XXKKHKKYDAEYYIENQVLP	AVLRILE	AX	FGY	RKEDLR
Hys1	XD	PKKHKKYDAEYYIENQVLP	AVLRILE	GG	FGY	RKEDLR
Hys2	FD	LKKHKKYDAEYYIENQVLP	AVLRILE	GG	FGY	RKEDLR
Hys3	FD	LKKHKKYDAEYYIENQVLP	AVLRILE	GG	FGY	RKEDLR
Hys4	FD	PKKHKKYDAEYYIENQVLP	AVLRILE	EG	FGY	RKEDLR
PhS1	YD	PKKHKKYDAEYYIENQVLP	AVLRILE	EG	FGY	RKEDLR
PhS2	YD	LKKHKKYDAEYYIENQVLP	AVLRILE	AF	FGY	RKEDLR
PhS3	YD	PKKHKKYDAEYYIENQVLP	AVLRILE	AF	FGY	RKEDLR
PhS4	YD	LKKHKKYDAEYYIENQVLP	AVLRILE	AF	FGY	RKEDLR
PhS5	YD	LKKHKKYDAEYYIENQVLP	AVLRILE	AF	FGY	RKEDLR
PhS6	YD	LKKHKKYDAEYYIENQVLP	AVLRILE	AF	FGY	RKEDLR
PhS7	YD	LKKHKKYDAEYYIENQVLP	AVLRILE	AF	FGY	RKEDLR

	790	800	810	820	830	840
Pfu						
DeepVent						
Hybrid_design						
HyS1	N H D					
Hyb2	G A T V K F K Y K G E E K E V D I S K I K K V W R V G K M I S F T Y D E G G G K T G R G A V S E K D A P K E L L Q M L E					
Hyb3						
HyS4	G A T V K F K Y K G E E K E V D I S K I K K V W R V G K M I S F T Y D E G G G K T G R G A V S E K D A P K E L L Q M L E					
PhS1	G A T V K F K Y K G E E K E V D I S K I K K V W R V G K M I S F T Y D E G G G K T G R G A V S E K D A P K E L L Q M L E					
PhS2						
PhS3	G A T V K F K Y K G E E K E V D I S K I K K V W R V G K M I S F T Y D E G G G K T G R G A V S E K D A P K E L L Q M L E					
PhS4	G A T V K F K Y K G E E K E V D I S K I K K V W R V G K M I S F T Y D E G G G K T G R G A V S E K D A P K E L L Q M L E					
PhS5						
PhS6	G A T V K F K Y K G E E K E V D I S K I K K V W R V G K M I S F T Y D E G G G K T G R G A V S E K D A P K E L L Q M L E					
PhS7						

Pfu
 DeepVent
 Hybrid_design
 HyS1
 Hyb2
 Hyb3
 HyS4
 PhS1
 PhS2
 PhS3
 PhS4
 PhS5
 PhS6
 PhS7

Figure 6



**Invariable sequence element (24 aa) in hybrid proteins
(contains nucleotide binding motif)**